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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,808	02/15/2005	Yunging Liu	JEEKP102US	1617

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,808	LIU ET AL.	
	Examiner	Art Unit	
	GOLLAMUDI S. KISHORE	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6-26-09 & 10-7-09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8 and 10-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendments dated 6-26-09 and 10-7-09 are acknowledged.

Claims included in the prosecution are 1-3, 5-8 and 10-16.

In view of the amendments, the 102 rejections are withdrawn.

Claim Rejections - 35 USC § 112

1. Claims 1-3, 5-8 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant amends claim 1 to introduce 'consisting of'. This expression is a closed expression and does not permit the addition of any other substance. A careful review of the specification including the examples indicates the presence of surfactants and stabilizers in the method. Therefore, the added expression is deemed to be new matter.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3, 5-8 and 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what applicant intends to convey by 'amphiphile is a combination of hydroxypropyl-beta-cyclodextrin and phospholipids' in claim 1. What is

meant by 'combination'? a complex? If it is simply a mixture, as pointed out before, compounds such as cyclodextrins which are not really amphiphiles.

'Consisting of' is a closed expression and does not permit the addition any other material. Therefore, step E in claim 1 is inconsistent with this expression. What is being conveyed by the expression, "solution is selected from hydrophilic solvent or a combination of hydrophilic solvent and water"? Furthermore, the distinction between a hydrophilic solvent and water is unclear. Water is a hydrophilic solvent. Additionally, the examiner points out that phospholipids being lipophilic, addition of a hydrophilic solvent or water would only form a suspension and not a solution.

It is unclear as to what applicant intends to convey by 'solid particles dissolve in water and form a microemulsion or submicroemulsion' in claim 2. If the solid dissolves then it is a solution and not an emulsion.

If the solid particles are steadily suspended in the water, how can the system be homogeneous system as recited in claim 3?

According to claim 1, the particle sizes are 1 nm to about 300 nm. Claim 8 recites the sizes as 'less than 300 nm' and thus, not further limiting claim 1 in terms of sizes.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 5-8 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/16196 cited in the previous action.

WO discloses solid formulations containing cyclodextrins and phospholipid and an active agent. One of the cyclodextrins taught is hydroxypropyl-beta-cyclodextrin. The ratio of the cyclodextrin to phospholipid is 1: 0.22. The formulations further contain polyvinylpyrrolidone. The method involves the addition of the active agent to the amphiphile followed by lyophilization (abstract, page 5, line 5; page 7, line 28, Examples and claims). Although WO discloses the formation of powdery formulations, it does not specify the sizes of the particles. What is also lacking in WO is the use of a lipophilic active agent such as taxol and the temperature at which the amphiphile is dissolved. However, since the dissolution of the amphiphile is important, it would have been obvious to one of ordinary skill in the art to use the proper temperature at which the amphiphile dissolves and therefore, deemed to be parameters manipulatable by an artisan. WO also does not explicitly state the sizes of the particles. In the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to manipulate the sizes to obtain the best possible results. Since WO's formulations are for the delivery of the active agents, it is deemed obvious to one of ordinary skill in the art to encapsulate any active agent with a reasonable expectation of success.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that WO teaches the use of alkyl ether of cellulose and instant claims recite 'consisting of' which excludes this compound. This argument is not persuasive. First of all as pointed out above, though claims now recite consisting of, they do recite

other compounds as optional. Secondly, claim 1 recites generic 'stabilizer' and applicant has not shown that the cellulose is not a stabilizer. Finally it should be pointed out that Example 1 on pages 11 and 12 of WO shows the presence of only the phospholipid and cyclodextrin and not a cellulose. With regard to arguments that WO lacks hydroxypropyl cyclodextrin, the examiner points out to page 5, line 5 of WO. With regard to ratios, the examiner points out to Example 1.

6. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92 cited above in view of Zou (5,902,604) cited above.

The teachings of WO have been discussed above. What is lacking in WO is the use of surfactant such as sorbitan 80 and povdone.

Zou discloses liposomal formulations containing a phospholipid, Sorbate 80 and an active agent. The active agents include anthracycline compounds such as doxorubicin and annamycin. The compositions further include polyvinylpyrrolidone. The method of preparation involves the preparation of a solution of the phospholipid in butyl alcohol and Water and the active agent is added to the phospholipid. The surfactant is added to the solution. The composition is then lyophilized (abstract, col. 2, lines 22-51; col. 3, line 3 through col. 5, line 34; col. 6, lines 59-67; Examples and claims). Zou in addition teaches that the addition of sorbitans not only stabilizes the liposomal composition, but also modulates the sizes of the liposomes (Discussion on col. 13).

The inclusion of a surfactant in the composition of WO would have been obvious to one of ordinary skill in the art since such an inclusion would stabilize the compositions, but also modulates the particle sizes as taught by Zou.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Zou does not teach a combination of hydroxypropyl-beta-cyclodextrin and phospholipids and the claimed features B-E. This argument is not persuasive since Zou is added for its teachings of surfactant and its ability to modulate the particle sizes and the primary reference teaches combining the cyclodextrin, phospholipid and the drug.

7. Claims 7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92 cited above in combination with Zadi cited in the previous action or Kim (5,759,573).

The teachings of WO have been discussed above. WO does not teach paclitaxel as the active agent. However, it would have been obvious to one of ordinary skill in the art to encapsulate paclitaxel with a reasonable expectation of success since Zadi teaches that phospholipid containing liposomes are routinely used for the encapsulation of paclitaxel.

Kim (5,759,573) teaches hydroxypropyl beta cyclodextrin-phospholipid complexes for the delivery of active agents such as taxol (abstract, col. 5, lines 1-30 and claims).

One of ordinary skill in the art would be further motivated to use taxol as the active agent in WO since the reference of Kim shows that phospholipid-hydroxypropyl beta cyclodextrin complex is routinely used for the delivery of active agents such as taxol.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GOLLAMUDI S. KISHORE whose telephone number is (571)272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612

GSK